

Remarks

Claims 1, 3-12, 14-17, and 19-24 are pending in this application. Claims 26-60 were earlier withdrawn from consideration as drawn to non-elected subject matter and are canceled herein for the same reason. Applicant respectfully reserves the right to file one or more continuing applications drawn to the subject matter of claims 26-60. Claims 1, 3-12, 14-17, and 19-24 are currently under consideration.

Claims 2, 15, 18, and 25 have been canceled and the subject matter thereof incorporated into claim 1. Applicant respectfully reserves the right to file one or more continuing applications for claiming the invention as originally claimed. Claims 3, 4, and 19-24 have been amended to correct the dependency thereof in view of cancellation of claims. Claims 5, 8, and 10 have been amended to omit the word "further" in view of the amendment to claim 1. Therefore, no new matter has been added to the application by virtue of these amendments. These amendments should be entered because they place the application in condition for allowance or at least in better condition for appeal.

I. Response to Rejections under 35 U.S.C. § 103

A. Legal Standards for Examination under Section 103

The legal standards for examination under 35 U.S.C. § 103 were reviewed in the response to the previous Office Action. That review is hereby incorporated by reference.

The Office Action cited *In re McLaughlin*, 443 F.2d 1392, 170 U.S.P.Q. 209 (C.C.P.A. 1971), as standing for the proposition that hindsight reasoning in making a judgment on obviousness is permissible so long as the hindsight reasoning takes into account only knowledge within the level of ordinary skill in the art at the time the invention was made and does not include knowledge gleaned only from the applicant's disclosure. In the first place, *McLaughlin* was a case where the appellant argued that references had been improperly combined to attempt to establish a *prima facie* case of obviousness. The court found that there was sufficient motivation in the prior art to make the combination of references. In *dictum* the court made the statement that the Office Action referred to about hindsight. Therefore, *McLaughlin* is *dictum* for the purpose for which the Office Action cited it. In the second place, a few years later the C.C.P.A. stated in *In re Carroll*, 202 U.S.P.Q. 571, 572 (C.C.P.A. 1979) :

One of the more difficult aspects of resolving questions of non-obviousness is the necessity "to guard against slipping into use of hindsight." *Graham v. John Deere Co.*, 383 U.S. 1, 36, 148 USPQ 459, 474 (1965). Many inventions may seem obvious to everyone after they have been made. However, 35 USC 103 instructs us to inquire

into whether the claimed invention "would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains." Thus, in deciding the issue of obviousness, we must look at the prior art presented from a vantage point in time prior to when the invention was made, and through the eyes of a hypothetical person of ordinary skill in the art.

Moreover, it has been widely recognized that virtually every invention is a combination of elements and that most, if not all, of these will be found somewhere in an examination of the prior art. This reasoning led the Federal Circuit, in *Connell v. Sears, Roebuck & Co.*, 220 U.S.P.Q. 193, 199 (Fed. Cir. 1983) to state:

The test is whether the claimed invention as a whole, in light of all the teachings of the references in their entireties, would have been obvious to one of ordinary skill in the art at the time the invention was made.

Still further, the Federal Circuit stated as follows:

It is essential that "the decisionmaker forget what he or she has been taught at trial about the claimed invention and cast the mind back to the time the invention was made . . . to occupy the mind of one skilled in the art who is presented only with the references, and who is normally guided by the then-accepted wisdom in the art." [W.L. Gore, 721 F.2d at 1553, 220 USPQ at 312-13.] One cannot use hindsight reconstruction to pick and choose among isolated disclosures in the prior art to deprecate the claimed invention.

In re Fine, 837 F.2d 1071, 5 USPQ2d 1596, 1599-1600 (Fed. Cir. 1988).

B. Factual and Legal Arguments

1. Claims 1-3, 8-9, and 13-24

Claims 1-3, 8-9, and 13-24 were rejected under 35 U.S.C. § 103(a) as allegedly being unpatentable over U.S. Patent No. 6,743,436 ("Lee") in view of U.S. Patent No. 6,383,471 ("Chen").

Lee discloses an anesthetic microemulsion composition for intravenous injection, which requires as essential ingredients propofol and a poloxamer, alone or in combination with another co-surfactant. (Col. 4, lines 17-19 and 49-52.) Co-surfactants consist of Solutol HS 15, egg lecithin, Labrasol, polyoxy 10 oleyl ether, Tween, ethanol, and polyethylene glycol. (Col. 4, lines 35-42.)

Chen discloses a pharmaceutical composition requiring as essential ingredients an ionizable hydrophobic therapeutic agent and a carrier. (Col. 2, lines 60-62; Abstr.) The carrier must contain a surfactant and an ionizing agent to ionize, and thus solubilize, the therapeutic agent. (Col. 2, lines 62-64; Abstr.) Optionally, the carrier also includes solubilizers, triglycerides, and neutralizing agents. (Col. 2, lines 64-65; Abstr.) The pharmaceutical composition is primarily designed for use in oral dosage forms (Col. 4, lines 62-64; Abstr.), although other dosage forms are not excluded (Col. 35, lines 9-23.) Propofol was included in a long (more than 4 columns) list of ionizable therapeutic agents (Col. 6, line 14, to col. 10, line 35).

Ionizing agents are disclosed as pharmaceutically acceptable acids or bases (Col. 11, lines 2-6.) Surfactants are disclosed as hydrophilic, hydrophobic, or a mixture of hydrophilic and hydrophobic surfactants. (Col. 13, lines 62-64.) Specific types and examples of surfactants are disclosed in long (16 columns) lists at col. 15, line 7, to col. 31, line 25.) Long lists of solubilizers and triglycerides are disclosed, as well. (Col. 31, line 40, to col. 34, line 45.)

Before continuing, it is necessary to comment on the following statement in the Office Action:

Applicant's state that the Lee et al. reference is drawn to making an injectable composition and teaches away from making a composition that lacks a poloxamer. This argument is not found to be persuasive because Lee et al. teach that the composition comprises the poloxamer. Comprising language means that all of the elements can be present or some of the elements may be present. Therefore, the reference does not rely upon a poloxamer.

(Office Action at page 2.) This is simply wrong. Numerous cases could be cited, but *Genentech Inc. v. Chiron Corp.*, 42 U.S.P.Q.2d 1608, 1613 (Fed. Cir. 1997) will suffice: "'Comprising' is a term of art used in claim language which means that the named elements are essential, but other elements may be added and still form a construct within the scope of the claims." See also, MPEP § 2111.03. Therefore, since Lee discloses an "anesthetic composition for intravenous injection, comprising propofol and a poloxamer" (e.g., col. 3, lines 8-11; claim 1; Abstract), a poloxamer is an essential element of Lee's invention. That is, Lee relies on a

poloxamer being present. In still other words, a poloxamer is critical to Lee's invention.

The Office Action alleged that it would have been obvious to combine the teachings of Lee and Chen to arrive at the presently claimed invention. While Lee is drawn to making an injectable composition, Chen is particularly directed to making an oral formulation. Further, Applicant could find no mention in these cited references of an object to formulate a clear composition or a disclosure of how to formulate a clear injectable composition. Moreover, Applicant respectfully submits the only mention of optical clarity of the presently claimed invention is found in Applicant's disclosure. The Office Action admitted that neither Lee nor Chen discloses optical clarity. Still further, the solubilizers of Chen's disclosure are optionally added to the combination of an ionizable hydrophobic therapeutic agent, an ionizing agent (which is added to solubilize the therapeutic agent by adjusting the pH of the solution to ionize the therapeutic agent; Col. 1, lines 40-43), and a surfactant to "enhance the solubility of the ionizable hydrophobic therapeutic agent in the carrier system (Col. 31, lines 40-43). Therefore, with respect to claim 1, the Office Action alleges that one would be motivated to pick propofol and solutol HS 15 from Lee and to pick tetrahydrofurfuryl alcohol polyethylene glycol ether ("glycofurool") from Chen, while ignoring the requirement for a poloxamer from Lee

and the requirement for an ionizing agent and a surfactant from Chen. The Office Action also appears to suggest that one would be motivated to make the necessary combination while ignoring the hundreds of other therapeutic agents, ionizing agents, surfactants, solubilizers, and triglycerides disclosed by Chen. The Office Action further suggests that one would be motivated to make a clear injectable composition by combining disclosures that do not mention optical clarity. The Office Action still further states that one would be motivated to combine an injectable composition with an oral composition to result in a clear microemulsion-containing composition. Applicant respectfully submits that it would not be obvious to a person of ordinary skill in the art to make the presently claimed composition from a combination of Lee and Chen. It would simply be too hypothetical to pick and choose ingredients, as proposed in the Office Action, to result in an optically clear microemulsion composition with a reasonable likelihood of success. Thus, a *prima facie* case of obviousness has not been established.

With all due respect, although the suggestion to combine references may flow from the nature of the problem, "[d]efining the problem in terms of its solution reveals improper hindsight in the selection of the prior art relevant to obviousness." *Monarch Knitting Machine Corp. v. Sulzer Morat GmbH*, 139 F.3d 877, 880, 4 U.S.P.Q.2d 1977, 1981 (Fed. Cir. 1998). Applicant respectfully submits that if one follows the above guidelines and analyzes the

art properly, then it would not be obvious to make the invention as claimed.

Still further, references must be considered as a whole, including subject matter that teaches away from the invention as well as subject matter that suggests the invention, and not for their isolated teachings. *Ashland Oil, Inc. v. Delta Resins & Refractories, Inc.*, 227 U.S.P.Q. 657, 669 (Fed. Cir. 1985). Lee teaches making an injectable composition that requires a combination of propofol and a poloxamer. Therefore, Lee teaches away from making a composition that lacks a poloxamer. Further, Chen teaches making an oral composition containing as essential ingredients an ionizable hydrophobic therapeutic agent (propofol is one of scores of such agents), an ionizing agent, and a surfactant. Optionally, a solubilizer (glycofurool is one of scores of such solubilizers), a triglyceride, and a neutralizing agent can also be included. Therefore, Chen teaches away from making a composition that contains glycofurool without also containing an ionizing agent and a surfactant and also ignores the option of adding a triglyceride and a neutralizing agent. Therefore, Applicant respectfully submits that the Office Action did not consider the cited references in their entireties, and the disclosures of the cited references that teach away from making the presently claimed invention were not given due consideration. For these reasons, a *prima facie* case of obviousness has not been established.

For these reasons, withdrawal of the rejections under Section 103 is respectfully requested.

2. Claims 4-7, 10-12, and 25

Claims 4-7, 10-12, and 25 were rejected under 35 U.S.C. § 103(a) as allegedly being unpatentable over Lee and Chen and further in view of US Patent Application Publication No. 20020107291 ("De Tommaso").

De Tommaso discloses an aqueous, clear, injectable pharmaceutical composition requiring as essential ingredients propofol, a pharmaceutically acceptable salt of a bile acid, and lecithin. (¶ 0005.) The disclosures of Lee and Chen were described above.

The defects in the *prima facie* case of obviousness against claims 1-3, 8-9, and 13-24 are also present here. The cited references were not considered in their entireties. It is not clear what combining a microemulsion (Lee), an oral formulation (Chen), and an injectable composition (De Tommaso) would be, but it would not be the presently claimed invention. Also, the cited references were not considered for their disclosures that teach away from making the presently claimed invention, as recited above. The motivation for picking and choosing among the hundreds of disclosed compounds is lacking or found only in Applicant's disclosure. Moreover, it is apparent that the conclusions of the

Office Action were arrived at using "hindsight reconstruction to pick and choose among isolated disclosures in the prior art to deprecate the claimed invention," *In re Fine*, 5 USPQ2d 1600, *supra*, which is inappropriate procedure for examining claims under accepted Section 103 jurisprudence. For these reasons, a *prima facie* case of obviousness has not been established. Withdrawal of the rejections is thus respectfully requested.

II. Conclusion

Should the Examiner deem it advisable to conduct a telephone interview for any reason, the undersigned attorney would be most agreeable to receiving a telephone call to expedite the prosecution of the application.

For the reasons given above, Applicant respectfully requests reconsideration and allowance of Claims 1, 3-12, 14-17, and 19-24 and passage of this application to issue.

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Respectfully submitted,



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